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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,224	06/22/2001	Jay M. Short	DIVER1150-6	8097

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EXAMINER

WHISENANT, ETHAN C

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 02/28/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,224	SHORT ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-92 is/are pending in the application.
- 4a) Of the above claim(s) 1-41 and 56-87 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-55 and 88-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. The applicant's election of Group IV (Claims 42-55 and 88-92) with traverse in paper no. 8 is acknowledged. Claims 1-41 and 56-87 are withdrawn from further consideration as being directed toward a non-elected invention.

It is noted that the applicant has traversed the restriction requirement, however, because the applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction requirement has been reconsidered, is deemed proper and is therefore, herein made **FINAL**.

SEQUENCE RULES

2. This application complies with the sequence rules and the sequences have been entered by the Scientific and Technical Information Center.

35 USC § 112 - 1ST PARAGRAPH

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

CLAIM REJECTIONS under 35 USC § 112- 1ST PARAGRAPH

4. **Claim(s) 88-92** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modifying SEQ ID NO: 1 and or close variants thereof which encodes a particular polypeptide; does not reasonably provide enablement for a method of modifying wherein **the polypeptide** to be modified is mixed with a small molecule to produce a modified small molecule. The specification does not enable any person skilled in the art to which it pertains, or with

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which it is most nearly connected to make the invention commensurate in scope with these claims without undue experimentation.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance presented as regards the how one is to produce a modified small molecule wherein a polypeptide with endoglucanase activity is mixed with a small molecule to produce a modified small molecule. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no showing as to how the method is to be accomplished beyond DNA mutagenesis. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. See M.P.E.P. §§ 706.03(n) and 706.03(z).

35 USC § 112- 2ND PARAGRAPH

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

6. Claim(s) 42-55 and 88-92 is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 it is unclear what is intended by the word "nucleotidesof" on line 5. The examiner has assumed that this is a misspelling of the phrase "nucleotides of". Please clarify.

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Claim 88 is indefinite because it is unclear as to how the method is to function. Note the 112, 1st paragraph rejection above.

35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

9. Claim(s) 42-55 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer [US 6,277,638 (2001)] in view of Knowles et al. [US 5,393,670 (1995)].

Claim 42 is drawn to a method of generating a variant which comprises two required steps. To begin, a nucleic acid - comprising a sequence as set forth in SEQ ID NO: 1, or sequences substantially identical thereto, or sequences complementary thereto or fragments comprising at least 30 consecutive nucleotides thereof or fragments comprising at least 30 consecutive nucleotides complementary thereto - is obtained. Next one or more nucleotides in said sequence are modified to another nucleotide or one or more nucleotides in said sequence are deleted or one or more nucleotides are added to said sequence.

Stemmer teaches a method of mutagenesis which comprises all of the limitations set forth in Claim 42 except these authors do not teach a nucleic acid as recited in Claim 42. However, Knowles et al. do teach a recombinant DNA vector encoding an endoglucanase and comprising a nucleic acid sequence substantially identical to that set forth in SEQ ID NO: 1. In addition, Stemmer teaches using his method (i.e. recursive DNA shuffling by fragmentation, reassembly and selection) to improve and/or optimize the yield, stability, and/or enzymatic capability of proteins. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Stemmer wherein the recombinant DNA vector encoding an endoglucanase and comprising a nucleic acid sequence substantially identical to that set forth in SEQ ID NO: 1 as taught by Knowles et al. was mutagenized. The motivation for making the modification recited above would have been to improve and/or optimize the yield, stability, and/or enzymatic capability of the endoglucanase taught by Knowles et al. Also, absent an unexpected result, the substitution of one known reagent with known properties for a second well known reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 43 is drawn to an embodiment of the method of Claim 42 wherein the modifications are introduced by a method selected from a defined group which includes error-prone PCR, and shuffling.

Stemmer et al. teaches these limitations. See, at least, for example, Claims 1 and 15-19.

Claim 44 is drawn to an embodiment of the method of Claim 42 wherein the modifications are introduced by error-prone PCR.

Stemmer et al. teaches this limitation. See, at least, for example, Claims 1 and 15-19.

Claim 45 is drawn to an embodiment of the method of Claim 42 wherein the modifications are introduced by shuffling.

Stemmer et al. teaches this limitation. See, at least, for example, Claims 1 and 15-19.

Claim 46 is drawn to an embodiment of the method of Claim 42 wherein the modifications are introduced by oligonucleotide-directed mutagenesis.

Stemmer et al. teaches this limitation. See, at least, for example, Claims 1 and 15-19.

Claim 47 is drawn to an embodiment of the method of Claim 42 wherein the modifications are introduced by assembly PCR.

Admittedly, Stemmer does not explicitly say assembly PCR, however, this limitation is, absent a showing to the contrary, considered to be inherent to Stemmer because recursive DNA shuffling by fragmentation, reassembly and selection is just that assembly PCR. In addition it has also been called sexual PCR mutagenesis by Stemmer. See Stemmer [US6,518,065 (2003)]. Also see, at least, for example, Claims 1 and 15-19 and Figure 1 of Stemmer [US 6,277,638 (2001)].

Claim 48 is drawn to an embodiment of the method of Claim 42 wherein the modifications are introduced by sexual PCR mutagenesis. Admittedly, Stemmer does not explicitly say sexual PCR mutagenesis, however, this limitation is, absent a showing to the contrary, considered to be inherent to Stemmer because recursive DNA shuffling by fragmentation, reassembly and selection is just that sexual PCR mutagenesis which also called assembly PCR. See, at least, for example, Claims 1 and 15-19 and Figure 1. Note also, Stemmer [US6,518,065 (2003)] wherein this author defines recursive DNA shuffling by fragmentation, reassembly and selection as being sexual PCR mutagenesis.

Claim 54 is drawn to an embodiment of the method of Claim 42 wherein the modifications are introduced by gene reassembly.

Stemmer et al. teaches this limitation. See, at least, for example, Claims 1 and 15-19.

Claims 49-53 and 55 are drawn to embodiments of the method of Claim 42 wherein the modifications are introduced by a particular type of mutagenesis, all of which were well known at the time of invention. Please note that, absent an unexpected result, the substitution of one method with known

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properties and outcomes for a second well known method with known properties and outcomes is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

CONCLUSION

10. Claim(s) 42-55 and 88-92 is/are rejected and/or objected to for the reason(s) set forth above.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.



Ethan Whisenant, Ph.D.
Primary Examiner